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Inhibition of Forskolin-induced Neurite Outgrowth and Protein Phosphorylation by a Newly Synthesized Selective Inhibitor of Cyclic AMP-dependent Protein Kinase, N-[2-(p-Bromocinnamylamino) ethyl]-5-isoquinolinesulfonamide (H-89), of PC12D Pheochromocytoma.

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To examine the role of protein kinase A in neurite outgrowth of PC12 cells, H-89 was applied along with nerve growth factor, forskolin, or dibutyryl cAMP. Pretreatment with H-89 led to a dose dependent inhibition of the forskolin-induced protein phosphorylation, with no decrease in intracellular cyclic AMP levels in PC12D cells, and the NGF-induced protein phosphorylation was not inhibited. H-89 also significantly inhibited the forskolin-induced neurite outgrowth from PC12D cells.

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Effects of Catecholamines and 4-Methylcatechol on the Synthesis and Secretion of Nerve Growth Factors by Rat Sciatic Nerve Segments in Culture.

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Epinephrine (EN), norepinephrine (NE), and dopamine (DA) separately increased the NGF content in both the conditioned medium (CM) and cultured rat sciatic nerve segments. The stimulation of the increase in NGF content was observed after an 8-h time lag. These observations suggest that catecholamines stimulate the *de novo* synthesis and secretion of NGF protein in organ culture. The maximal effects were observed at limited concentrations such as 0.1-0.2 mM and weakened after 2 days. A similar effect was observed with 4-methylcatechol, a non-amine catechol compound, but not with adrenergic α or β agonists, indicating that adrenergic receptors do not participate in effect.

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Stimulation of Nerve Growth Factor Synthesis/Secretion by 1,4-Benzoquinone and Its Derivatives in Cultured Mouse Astroglial Cells,

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Previously we reported that astroglial cells cultured from mouse brain synthesize and secrete NGF and that, in quiescent cells, catecholamines markedly increase the NGF content in the conditioned medium (CM). We wished to further assess the structural properties required for exhibition of such effect of compounds containing a ring structure analogous to that of catechol on astroglial NGF synthesis. During our study, we found that hydroquinone, which was confirmed to stimulate NGF synthesis in mouse fibroblast cells in another of our investigations, is a potent stimulator of NGF synthesis in astroglial cells and 1,4-benzoquinone is a more effective stimulator.